REMARKS/ARGUMENTS

In response to the Rejection mailed June 22, 2006, Applicants have amended claims 1, 29, 37-40 and 56, and present the following remarks. Claims 1-4, 6-23, 29, 37-40 and 54-57 are pending. Claims 5, 24-28, 30-36 and 41-53 have been canceled.

Applicants appreciate the examiner noting certain objection and rejections are withdrawn.

Claims 1-4, 6-23, 29, 37-40 and 54-56 were rejected under 35 USC 112, first paragraph, as the specification does not enable the present claims. The examiner objects to the use of the term "vaccine". It is clear the examiner's definition of the term is different from that used in applicants specification's "Definitions" section. To expedite prosecution, the term has been deleted from claims 1, 29, 37-40 and 56. However, it is to be understood that the claimed compositions are to be used as a vaccine as defined in applicant's specification. Accordingly, the rejection should be withdrawn.

Claims 1-4, 6-23, 29, 37-40 and 54-56 were rejected under 35 USC 112, first paragraph, as the specification does not enable the present claims to recite using an epitope which is less than the idiotype expressed on the surface of B-cell lymphomas. Applicants intend to claim compositions that have sufficient epitopes to induce the appropriate immune response. While applicants have compositions, which have at least the tumor surface Ig idiotype, applicants have not performed the extensive experimentation needed to state exactly which epitope(s) constitute the appropriate idiotypic portions of the antigens.

The specification describes and defines the idiotype as containing the epitopes needed to elicit the anti-tumor immune response. See the discussion in the specification on page 2, page 13, lines 21+, page 16 second paragraph and many other locations. Also note that claim 1 (line 1) is a "self-antigen" and the definition of "self antigen" in the paragraph bridging pages 16 and 17 also discusses what constitutes the idiotype needed.

Therefore, claims reciting the tumor "idiotype" would encompass whatever epitopes are required to elicit the immune response without requiring a particular chemical compound. The claims have been so amended. In view of the Examiner's usage of the term anti-idiotypic antibodies, it appears he should consider this amendment acceptable.

Claims 54 and 56 were rejected under 35 USC 112, first paragraph, as the specification as not complying with the written description requirement.
The recitations reciting an adjuvant not being present are considered "new matter". The examiner contends that plant expression systems produce the inherent immunogenicity of the polypeptide produced and that is not claimed. This rejection is respectfully traversed.

While the polypeptides of the present invention were produced by plant expression systems, it is unknown whether this is entirely responsible for the polypeptide being correctly folded without need for denaturation and renaturation. The generation of many different linkers through a semi-randomization process also allows great flexibility in the structure of the polypeptide and may be responsible for the correctly folded nature of the polypeptide and the corresponding inherent immunogenicity without an adjuvant. Either way, it is the correctly folded nature of the polypeptide that is in part responsible for the polypeptides immunogenicity. Claim 1, (c) and (d) recite these features. Also, the specification adequately demonstrates using the polypeptide without an adjuvant. Accordingly, the rejection should be withdrawn.

Claims 1-4, 6-13, 17-23, 29 and 38 were rejected under 35 USC 102(b) as being anticipated by Caspar et al. The examiner contends that an in-vivo produced polypeptide is the same as that claimed. This rejection is respectfully traversed.

The examiner asserts that the Caspar et al composition scFv (adenovirus) expresses the same polypeptide in vivo. Whether true or not, that particular Caspar et al composition is an adenovirus, not a polypeptide. The claims recite a purified polypeptide composition, not an adenovirus. Even if the exact same active molecule is produced in vivo using the Caspar et al adenovirus, that still does not anticipate the claimed

composition. The claimed composition is purified (claim 1, line 1) whereas Caspar et al's would not be. The claimed composition also induces an immune response in a mammal claim 1(d). The in-vivo composition in Caspar et al is an immunized mouse. A whole mouse is neither a purified polypeptide nor is it capable of inducing an immune response (without some type of treatment).

Mice that produce anti-idiotypic antibodies would have cleared the adenovirus and any produced self-antigen polypeptide and thus the recited polypeptide would not be present. Therefore, the examiner's argument that the polypeptide is inherently present also is not expected to be accurate.

The examiner also argues the language "includes..." as being open. However, this claim language was previously canceled and is not present in the present claims. Accordingly, this rejection should be withdrawn.

Claims 1-4, 6-12, 17-23, 29 and 37-38 were rejected under 35 USC 102(b) as being anticipated by Hawkins et al. The examiner contends that polypeptide Hawkins et al teach is the same as that claimed. This rejection is respectfully traversed.

The claims are directed to a purified polypeptide whereas Hawkins et al teach immunizing with a nucleic acid. These are technically different compounds.

Nucleic acid immunization does not produce necessarily produce the same type of immune response. See Caspar et al, figure 2 and 4 where it is different from polypeptide immunization. Therefore, the nucleic acid immunization of Hawkins et al is likely to produce a functionally different response as compared to polypeptide immunization.

Still further where does Hawkins et al demonstrate a purified polypeptide with any immunizing activity at all? Until that can be shown, Hawkins et al cannot be said to teach a polypeptide which can immunize without an adjuvant, a feature of claim 1(d). Accordingly, the rejection should be withdrawn.

Claims 1-4, 6-23, 29, 37-40 and 54 were rejected under 35 USC 103 as being unpatentable over Caspar et al in view of Fiedler et al, Tang et al and Hakim et al.

Caspar et al was applied above. The basis for the rejection is basically the same as previously. This rejection is respectfully traversed.

On page 14, lines 6-7 of the rejection, the examiner rejects the applicants arguments because:

> *"Applicant's arguments are not commensurate in scope with the claims. Again the claimed polypeptide self-antigen "includes...", which is synonymous to "comprising" and is inclusive or open-ended..."*

Claim 1 has been amended and the language "includes..." has been removed. Therefore, the basis for the rejection has been overcome and the rejection should be withdrawn.

The examiner has repeated many arguments related to Fiedler et al and Tang et al but these completely miss the point of the invention. Fiedler et al and Tang et al produce similar molecules for binding or enhanced binding. This is completely different from producing similar molecules for immunization. For example, it is a requirement that peptide folding mimic the natural tumor antigen in order for the peptide to be an effective vaccine. However for binding assays, a peptide (scFv) which folds slightly differently is acceptable provided it binds, and since it may binds stronger, a different folding may be preferable. Also, for example, polypeptide solubility in body fluids is believed to affect vaccine effectiveness. However, solubility does not significantly affect binding ability a common immunoassay sandwiches the antigen between a labeled antibody (soluble) and an antibody (insoluble) immobilized on a solid phase (bead or inner side of a tube or multiwelled plate).

Following the Fiedler et al teaching to produce a scFv for a binding immunoassay would not likely produce the claimed invention. Following the Tang et al teaching to produce a high affinity scFv would not likely produce the claimed invention either. Both references teach methods likely to be inoperable for making B-cell lymphoma vaccines because both references select for a scFv that is usually inoperable for vaccine purposes. As explained below, selection for high binding affinity is to the detriment of selecting for immunogenicity.

B-cells are a population of slightly different clonal cells where each clone of B-cells is capable of producing a different antibody (or surface immunoglobulin). Some of

these antibodies have low binding affinities, some have medium binding affinities and some have high binding affinities. The B-cell clones have a wide distribution of binding affinities.

Most antibody molecules are not high affinity binders. (side note: even the Federal Circuit has recognized this notion in the reasons for why U.S. Patent **4,376,110** was held patentable in Hybritech v. Monoclonal Antibodies.) The Tang et al reference uses extensive modification and screening 10^7 clones in order to get one with high binding affinity. With few high binding affinity scFv produced, this alone suggests that well over 99% of the clones were discarded as less than high affinity binders.

B-cell lymphomas result from a B-cell becoming a tumor. There is no particular reason to expect this B-cell tumor to produce a high affinity antibody/surface immunoglobulin. In the present invention, applicants wish to mimic the tumor's surface immunoglobulin. If one were to select a scFv with a high affinity, such as by employing it in an assay taught by Fiedler et al or Tang et al, then one is usually selecting for properties different from and at the expense of those needed for vaccine purposes.

The examiner is correct that applicants have the burden of showing that the scFv polypeptide produced by the prior art is different from that claimed. However, there still must be a reason to expect that the techniques used in the combination of references will produce the claimed composition. Because the goals and claimed properties are different from those expected to be produced by process such as Fiedler et al and Tang et al, one skilled in the art would not expect the proposed combination of teachings used in the rejection to yield an effective vaccine.

The rejection still lacks any clear teaching that an effective scFv vaccine can be made by a plant cell. The rejection still lacks any clear teaching that linker optimization will produce a scFv that more closely mimics a B-lymphoma surface idiotype antigen.

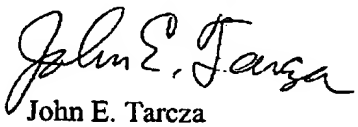
Accordingly, for the above and previously presented reasons, the combination of references does not reasonably suggest or motivate one to produce the claimed purified polypeptide self-antigen with the claimed properties.

In view of the above amendments and comments, the claims are now in condition for allowance and applicants request a timely Notice of Allowance be issued in this

application. If needed, applicants petition for sufficient extension of time for consideration of this paper.

The commissioner hereby is authorized to charge payment of any fees, including extension of time fees, under 37 CFR § 1.17, which may become due in connection with the instant application or credit any overpayment to Deposit Account No.500933.

Respectfully submitted,



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